[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, HHS

ACTION: Notice

SUMMARY: The inventions listed below are owned by an agency of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

FOR FURTHER INFORMATION: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: 301-496-7057; fax: 301-402-0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Novel Analogues of the Asthma Drug Fenoterol as Liver and Brain Cancer Therapeutic Agents

Description of Technology: Available for licensing are specific fenoterol analogues, such as MNF, that inhibit the growth of various types of cancers, including brain, liver, colon, and lung tumors. MNF acts as an agonist of the GPRSS cannabinoid (CB) receptor and, as such, represents one of the first potential drugs directed at this target. MNF crosses the blood brain barrier and initial toxicity studies indicate that it has few off-target effects. These new analogues can be used to treat CB receptor related disorders and diseases, and in particular GRPSS-related disorders and diseases, including brain and liver cancers for which there are no current effective treatments.

Potential Commercial Applications:

• A new class of compounds that can be used to treat cannabinoid receptor related disorders and diseases.

• Treatments for liver, brain, colon, and lung cancers.

Competitive Advantages:

• Able to cross the blood:brain barrier.

• Few side-effects.

• Broad range of therapeutic activity.

• Can be formulated for oral administration.

Development Stage:

• Pre-clinical

• In vitro data available

• In vivo data available (animal)

Inventors: Irving Wainer, Michel Bernier, Rajib Paul (all of NIA)

Publications:

1. Paul RK, et al. Cannabinoid receptor activation correlates with the pro-apoptotic action of the beta2-adrenergic agonist (R,R')-4'-methoxy-1-naphthylfenoterol. J Pharmacol Exp Ther., in press.

2. Paul RK, et al. Negative regulation of GPR-55-mediated ligand uptake and cellular motility by (R,R')-4'-methoxy-1-napthylfenoterol. Br J Pharmacol., in preparation.

3. Paul RK, et al. The role of GPR55 and apoptotic signalling pathways in (R,R')-4'-methoxy-1-naphthyfenoterol. Cancer Res., in preparation.

Intellectual Property: HHS Reference No. E-139-2012/0 — U.S. Provisional Application No. 61/651,961 filed 25 May 2012

Licensing Contact: Patrick McCue, Ph.D.; 301-435-5560; mccuepat@mail.nih.gov

Collaborative Research Opportunities: The IRP/NIA/LCI is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize (R,R')-4'-methoxy-1-naphthylfenoterol for the treatment of brain, liver and colon carcinomas. For collaboration opportunities, please contact Nicole Guyton, Ph.D. at darackn@mail.nih.gov.

High-Affinity Mouse Monoclonal Antibodies to Glypican-3 (GPC3) for Research Use

Description of Technology: Liver cancer is the fifth most common cancer in the world, with hepatocellular cancer (HCC) representing the preponderance of these liver cancers. As with many cancers, positive prognosis for a patient diagnosed with HCC correlates with the early detection of the disease. Unfortunately, HCC is usually detected at a late stage in its development, leading to poor prognosis for most patients. As a result, there is great interest and value in developing new agents which can detect the presence of HCC in a patient at an early stage.

Glypican-3 (GPC3) is a cell surface heparan sulfate glycoprotein that is expressed on the vast majority of HCC cells. The correlation between GPC3 expression and HCC makes GPC3 an attractive candidate for studying the disease progression and treatment of HCC. The presence, progression and treatment of this disease can potentially be monitored by tracking the level of expression of GPC3 on cells. This can be accomplished using monoclonal antibodies which recognize only GPC3, particularly the cell surface domain of the protein. This invention concerns the generation of several monoclonal antibodies that are specific for the cell surface domain of GPC3 (YP6, YP7, YP8, YP9 and YP9.1), and which can be used as research reagents for studying the role of GPC3 in HCC.

Potential Commercial Applications: Antibodies for use as research materials, including:

• detection of cells that express GPC3 for monitoring HCC disease progression and treatment

• immunostaining for tumor imaging

• ELISA and immunohistochemistry applications

• any other antibody-related research use, including immunoprecipitation, western blot analysis, etc.

Competitive Advantages:

• Higher binding affinity (subnanomolar levels) than commercially available GPC3 antibodies such as 1G12

• Recognition of cells with low levels of GPC3 expression

• Able to bind to wild-type GPC3 (conjugated to heparan sulfate) better than the GPC3 core protein (lacking heparan sulfate)

Development Stage:

• Early-stage

• In vitro data available

Inventors: Mitchell Ho et al. (NCI)

Publications:

1. Ho M, Kim H. Glypican-3: a new target for cancer immunotherapy. Eur J Cancer. 2011 Feb;47(3):333-338. [PMID 21112773]

2. Ho M. Advances in liver cancer antibody therapies: a focus on glypican-3 and mesothelin. BioDrugs. 2011 Oct 1;25(5):275-284. [PMID 21942912]

Intellectual Property: HHS Reference No. E-136-2012/0 — U.S. Provisional Application No. 61/654,232 filed 01 Jun 2012

Related Technology: HHS Reference No. E-130-2011/0 — U.S. Provisional Application No. 61/477,020 filed 19 Apr 2011; PCT Application No. PCT/US2012/034186 filed 19 Apr 2012

Licensing Contact: David A. Lambertson, Ph.D.; 301-435-4632; lambertsond@mail.nih.gov

Collaborative Research Opportunity: The National Cancer Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize cancer diagnostics, isolation of circulating tumor cells, humanization and/or immunoconjugates. For collaboration opportunities, please contact John Hewes, Ph.D. at hewesj@mail.nih.gov.

Self-Assembled Ferritin Nanoparticles Expressing Hemagglutinin as an Influenza Vaccine

Description of Technology: NIH inventors at the Vaccine Research Center have developed a novel influenza virus hemagglutinin (HA)-ferritin nanoparticle influenza vaccine that is easily manufactured, potent, and elicits broadly neutralizing influenza antibodies against multiple strains of influenza. This novel influenza nanoparticle vaccine elicited two types of broadly neutralizing, cross-protective antibodies, one directed to the highly conserved HA stem and a second proximal to the conserved receptor binding site (RBS) of the viral HA, providing a new platform for universal and seasonal influenza. In addition, HA-ferritin nanoparticles can be easily produced from simple expression vectors and without the production of infectious virus in eggs, and will facilitate influenza preparedness in the face of emerging epidemics.

This technology exploits ferritin, a ubiquitous iron storage protein, that self-assembles into spherical nanoparticles and could serve as a scaffold to express a heterologous protein, such as influenza HA, so it mimics a physiologically relevant

trimeric viral spike. Immunization with the HA-ferritin nanoparticle elicited neutralizing antibody titers that were >10-fold higher than a matched inactivated vaccine. The immune sera raised by HA-ferritin nanoparticles expressing a 1999 HA neutralized seasonal H1N1 viruses from 1934 to 2007 and protected ferrets from an unmatched 2007 H1N1 virus challenge. This extended neutralization coverage is partially explained by the presence of both type of antibodies, antibodies directed to the conserved HA stem and against the RBS region. Finally, this ferritin nanoparticle vaccine platform has significant advantages in the ability to utilize specific multimerized spikes and it may be applicable to other viral proteins.

Potential Commercial Applications: The ferritin nanoparticles as a vaccine platform can be used to deliver vaccines, such as influenza vaccines, with enhanced magnitude and breadth of the neutralizing antibody responses. This vaccine platform may be applicable to other viral proteins.

Competitive Advantages:

• Forms an octahedron consisting of 24 subunits, allowing for greatly increased presentation of heterologous protein on the ferritin nanoparticles surface, compared to other vaccine platforms.

• *In vivo* data in multiple animal models demonstrated induction of broader and more potent antibody responses.

• Vaccine stimulated broadly neutralizing antibodies against the highly conserved epitope on the HA stem region and against the RBS, thus targeting two independent sites of vulnerability on HA.

• Multivalent influenza HA ferritin vaccines have been tested in animal models.

• Ferritin is extremely stable to temperature ranges, pH, detergent and other factors.

• Easily manufactured, will facilitate influenza preparedness in the face of emerging epidemics.

Development Status:

• Preclinical

• In vitro data available

• In vivo data available (animal)

Inventors: Gary Nabel, Masaru Kanekiyo, Jeffrey C. Boyington, Patrick McTamney (all of NIAID)

Publication: Kanekiyo M, et al. A Self-Assembling Influenza Nanoparticle Vaccine Elicits Two Types of Broadly Neutralizing and Cross-protective Antibodies. Manuscript submitted.

Intellectual Property:

• HHS Reference No. E-293-2011/0 — U.S. Provisional Application No. 61/538,663 filed 23 Sep 2011

• HHS Reference No. E-293-2011/1 — U.S. Provisional Application No. 61/661,209 filed 18 Jun 2012

Licensing Contact: Cristina Thalhammer-Reyero, Ph.D., M.B.A.; 301-435-4507; ThalhamC@mail.nih.gov

Salen-Manganese Compounds for Therapy of Viral Infections

Description of Technology: Salen-manganese compounds are synthetic, stable, low toxicity, low cost agents that may provide protection from immune reaction-related oxidative cell damage associated with many illnesses. In particular, oxidative cell damage has been associated with many viral infections including influenza. This invention demonstrates that treating mice with salen-manganese compounds, after lethal pandemic influenza virus infection, significantly enhances survival. Salen-manganese treatment also reduces lung pathology and also improved cellular recovery and repair. Because oxidative damage is observed in many viral infections, administration of salen-manganese compounds may have therapeutic relevance to a wide range of viral infections, in addition influenza. Existing viral therapeutics merely target the infectious viral agent and not the damage caused by the immune system reaction related to infection. Because, salen-manganese treatments target the untapped therapeutic space of infection-induced, immune system-related pathology and have favorable safety and cost profiles, such therapies are ideal candidates for development.

Potential Commercial Applications: Viral therapeutics.

Competitive Advantages: Synthetic, stable, low toxicity, low cost, untapped therapeutic target space.

Development Stage:

• Early-stage

• Pre-clinical

• In vivo data available (animal)

Inventors: John Kash (NIAID), Jeffrey Taubenberger (NIAID), Rodney Levine (NHLBI), Susan Doctrow (Boston University)

Publications:

1. Doctrow SR, et al. Salen Manganese Complexes: Multifunctional Catalytic Antioxidants Protective in Models for Neurodegenerative Diseases of Aging. In: Medicinal Inorganic Chemistry, ACS Symposium Series, Vol. 903, Chapter 18, pp 319-347; August 25, 2005. [DOI: 10.1021/bk-2005-0903.ch018.]

2. Schwarz KB. Oxidative stress during viral infection: a review. Free Radic Biol Med. 1996;21(5):641-9. [PMID 8891667]

Intellectual Property: HHS Reference No. E-281-2011/0 — U.S. Provisional Application No. 61/558,137 filed 10 Nov 2011

Licensing Contact: Tedd Fenn, J.D.; 301-435-5031; Tedd.Fenn@nih.gov

Collaborative Research Opportunity: The NIAID Laboratory of Infectious Diseases, Viral Pathogenesis and Evolution Section, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize this technology. For collaboration opportunities, please contact Maryann Puglielli at 301-594-6656.

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Date

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Richard U. Rodriguez, M.B.A.
Director
Division of Technology Development and Transfer
Office of Technology Transfer
National Institutes of Health

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